Formulation and Evaluation of Buccal Filmsloaded with *Passiflora Incarnata* Extract

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ABSTRACT:
Mucoadhesive buccal films of Passiflora incarnata extract were prepared for the prevention and treatment of Anxiety. Films of varying polymeric composition were prepared in order to facilitate initial as well as prolonged drug release that could take care of acute as well as delayed emesis. Mucoadhesive buccal films were prepared using polymers such as ethyl cellulose and HPMC. The effect of concentration of these polymers on physical properties and drug release were studied. All the buccal films were prepared by solvent casting method. In another part of the study, the effect of drug concentration on physical and mucoadhesive properties of film were assessed, keeping the polymer concentration fixed. Buccal film containing Ethyl cellulose showed good mucoadhesion. The study concluded that the developed buccal films have the potential to release Passiflora incarnata required for anxiety, insomnia, and gastrointestinal distress.
Key words: Mucoadhesive buccal film, Passiflora incarnata , synthetic polymers, solvent casting technique, Diffusion mechanism.

I. INTRODUCTION

Buccal drug delivery offers an advantageous alternative by allowing the drug to be absorbed directly through the mucosal lining of the cheek, bypassing hepatic first-pass metabolism and offering a faster onset of action.[1]Buccal films, a modern dosage form, are thin, flexible, and mucoadhesive strips that can be easily applied to the buccal mucosa. They offer numerous benefits including improved patient compliance, accurate dosing, ease of administration without water, and sustained or controlled drug release.[2]*Passiflora incarnata* , commonly known as passionflower, is a well-known medicinal plant traditionally used for its anxiolytic, sedative, and anticonvulsant properties.[3] The active constituents of *Passiflora incarnata* , including flavonoids and alkaloids, contribute to its CNS depressant action and therapeutic potential in conditions such as anxiety, insomnia, and nervous disorders.[4] In this study, an attempt is made to formulate and evaluate buccal films containing *Passiflora incarnata* extract, aiming to enhance its therapeutic effectiveness, ensure rapid onset, and improve bioavailability through the buccal mucosa. Various film-forming polymers, plasticizers, and permeation enhancers are explored to achieve optimal film properties and drug release profiles.

II. EXPERIMENTAL WORK

MATERIALS

Passiflora incarnate Extract, HPMC Ethyl cellulose was obtained from Synpharma Research Labs, Hyderabad. Other chemicalsand the reagents used were of analytical grade.

METHODOLOGY

Compatibility studies of drug and polymers:[6]

In the formulation of *Passiflora incarnata* Extract Film formation, API and Excipient may interact as they are in close communication with each other, which could lead to the instability of drug. FT-IR spectroscopy was employed to ascertain the compatibility between *Passiflora incarnata* Extract and the selected polymers. The pure drug and drug with excipients were scanned separately.

***Passiflora incarnata* extract process[7]**

Collection and authentication of plant material

In the present study, the flowers of Passiflora Incarnata were collected from the Thirupathi. The plants were authenticated by Dr. Madhavan Chetty, Assistant Professor, Sri Venkateswara University, Tirupati, Andhra Pradesh, India. With the voucher no. 2071.The flower of Passiflora Incarnata were then washed with water to remove physical impurities like soil and dirt, dried at room temperature.

Soxhlet Extraction

Use dried, powdered *Passiflora incarnata* leaves (30–50 g).Load the powder into a thimble and place it in the Soxhlet extractor.Use Methanol (95%) solvent as the extracting solvent.Allow extraction to proceed for 6–8 hours or until the solvent in the siphon becomes colorless.Collect the extract and evaporate the solvent using a rotary evaporator.Dry and store the

extract in an amber vial under refrigeration (4–8°C).

Formulation design

Preparation of buccal films:

Table-1: Formulation Design of *Passiflora incarnata* ExtractBuccal films

F. Code	Extract(mg)	HPMC (mg)	Ethyl cellulose (mg)	Propylene glycol (ml)	Methanol (ml)	Aspartame (mg)
F1	20	100	-	2	5	2
F2	20	200	-	2	5	2
F3	20	300		2	5	2
F4	20	400		2	5	2
F5	20	-	100	2	5	2
F6	20	-	200	2	5	2
F7	20	-	300	2	5	2
F8	20	-	400	2	5	2

Solvent casting technique

Dissolve film-forming polymer(s) in the appropriate solvent.Stir continuously (magnetic stirrer/hotplate) until a clear, homogenous solution forms. Add the plasticizer to improve the flexibility and prevent brittleness of the filmStir the mixture until uniformly dispersed.Add the *Passiflora incarnata* extract to the polymer-plasticizer mixture.Mix gently to avoid foaming and ensure uniform distribution of the extract.Add sweetener (aspartame). Allow the solution to stand to remove entrapped air bubbles.Pour the final homogenous solution into a clean petri dish. Spread uniformly using a casting knife or film applicator to maintain consistent thickness.Allow the film to dry at controlled temperature (usually 40–50°C) in a hot air oven or at room temperature in a dust-free environment.Drying time may vary (typically 24–48 hours).Once dried, carefully peel off the film and cut it into uniform strips of desired size (e.g., 2 cm x 2 cm).Store in moisture-proof, airtight packaging (e.g., aluminum pouches) to protect from humidity and light.[8]

Evaluation of mucoadhesive buccal film formulation:

Physico- chemical evaluation:

Physical appearance:[9]

All the prepared mucoadhesive buccal films were observed for color, clarity, flexibility, and smoothness.

Folding endurance:[10]

Folding endurance Folding endurance value was calculated by folding the film of suitable size at the same place and counting the number of time the film could be folded without breaking. Swelling study: Percentage of hydration and matrix erosion Film swelling properties and erosion characteristics were determined by calculating the percentage of hydration and matrix erosion of the films. Films of definite size (1 × 1 cm2) were cut and weighed (W1). Film was placed on a weighed stainless steel wire mesh. The wire mesh and the film were immersed in phosphate buffer saline (pH 6.8) for predetermined time periods (1,2,3,4,5,6,7 and 8hrs.). At these time intervals the wire mesh was withdrawn from the buffer, the films were wiped off using filter paper and weighed (W2). Percentage hydration of the films was determined using the following relation:

Thickness of the film:[11]

The thickness of each film was measured by using screw gauze. The thickness was measured at three different places on each film and the average thickness of the film was taken as the thickness of the film.

Weight uniformity:[12]

The study of uniformity of drug content was done by spectrophotometric method. For this measurement a circular disc of films of 3 cm diameter without BOPP membrane was used. The films were initially extracted for *Passiflora incarnata* Extract by dissolving in a 100 mL volumetric flask containing mixture of ethanol and Phosphate buffer (pH 6.8) (20:80) for 12 h by intermittent sonication. The solution of buccal films was filtered by 0.45µm cellulose membrane filter and estimated for the content of drug by UV spectrophotometric measurement at 289 nm (Shimadzu 1800, Japan). The average of result was obtained from three consecutive determinations.

Drug content:[13]

To ensure the uniformity of distribution of *Passiflora incarnata* Extract in the film, a content uniformity test was done. Films (1 × 1 cm2 equivalent to 2 mg of *Passiflora incarnata* Extract) were cut at three different locations and dissolved in 10 ml of phosphate buffer saline (pH 6.8) by continuous shaking on a water bath at room temperature for 8 h. The solution was filtered through Whatman filter paper and the samples were diluted suitably and analyzed using UV spectrophotometer at a

λmax 289 nm against a blank (UV-1800, Double Beam spectrophotometer, LABINDIA).

Measurement of swelling index :[14]

This measurement is used to determine the extent of water uptake or the degree of hydration by the hydrophilic polymers used in the fabrication of the films. Most of the mucoadhesive polymers undergo some degree of swelling after hydration, which is necessary to initiate intimate contact of the film with the mucosal surface. The studies for determination of the Swelling Index of the films were conducted in the simulated salivary fluid of pH 6.8. The film sample (surface area : 1.75 cm^2) was weighed and placed in a preweighed stainless steel wire sieve of approximately 800 μm mesh. The mesh containing the film sample was then submerged in 15 mL of the simulated salivary medium contained in a porcelain dish. At definite time intervals, the stainless steel mesh was removed from the dish and the excess moisture was removed by carefully wiping it off with absorbent tissue, after which it was reweighed. Increase in weight of the film was determined at each time interval until a constant weight was observed. The degree of swelling was calculated using the formula:

$S.I = (w_t - w_0) / w_0$

where

S.I is the Swelling Index,

w_t is the weight of film at time 't' and

w_0 is the weight of the film at time 0.

Moisture absorption studies:[15]

The buccal films were weighed accurately and placed in the desiccators containing 100 ml of saturated solution of aluminum chloride, which maintains 76% and 86% relative humidity (RH). After 3 days, the films were taken out and weighed. The percentage moisture absorption was calculated using the formula:

$$\text{Perentage moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Moisture loss studies: [16]

The buccal films were weighed accurately and kept in desiccators containing anhydrous calcium chloride. After 3 days, the films were taken out and weighed. The moisture content (%) was determined by calculating moisture loss (%) using the formula:

$$\text{Percentage moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

***In-vitro* Drug release studies:**[17]

The commercially available dialysis membrane (obtained from Sigma Chemicals) was employed for the study, and the *in vitro* drug release study was carried out using a Franz diffusion cell. The effective diffusion area was 1.8 cm^2. The receptor compartment (40 ml) was filled with phosphate buffer saline (PBS), pH 6.8. The films were applied under occlusion on the dialysis membrane fitted between the donor and receptor compartments of the diffusion cell. The drug release was performed at 37 ± 0.5°C, at a stirring speed of 50 rpm using a magnetic stirrer. Five milliliters of the sample from receptor medium was withdrawn at regular intervals and replaced immediately with an equal volume of phosphate buffer saline, pH 6.8. The amount of *Passiflora incarnata* Extract released into the receptor medium was quantified by using UV–visible spectrophotometer at 289 nm against a blank.

Drug release kinetics[18]

In order to predict and correlate the release behavior of *Passiflora incarnata* Extract from different films, it is necessary to fit into a suitable mathematical model. The *in vitro Passiflora incarnata* Extract release data from buccal films were evaluated kinetically using various mathematical models like zero-order, first-order, Higuchi, and Korsmeyer–Peppas model equations.

Zero-Order Kinetics

$F = K_o t$, where F represents the fraction of drug released in time t, and K_o is the zero-order release constant.

First-Order Kinetics

$\ln(1 - F) = -K_1 t$, where F represents the fraction of drug released in time t, and K_1 is the first-order release constant.

Higuchi Model

$F = K_H t^{1/2}$, where F represents the fraction of drug released in time t, and K_H is the Higuchi dissolution constant.

Koresmeyer–Peppas Model

$F = K_p t^n$, where F represents the fraction of drug released in time t, K_p is the Koresmeyer–Peppas release rate constant, and n is the diffusion exponent.

The results of curve fitting into these above-mentioned mathematical models indicates the drug release behavior from these formulated buccal films of *Passiflora incarnata* Extract. When the release rate of *Passiflora incarnata* Extract and their respective correlation coefficients were compared, it was found to follow first-order release kinetics ($R^2 = 0.9866$ to 0.9984).

Stability studies:[19]

Optimized medicated films were subjected to short term stability testing. The buccal films were sealed in aluminium foils and kept in a humidity chamber maintained at 40 ± 2 ^{0}C and 75 ± 5% RH for 3 month as per ICH guidelines. Changes in the appearance and drug content of the stored films were investigated after storage at the end of every month.

III. RESULTS AND DISCUSSION

FT-IR Spectrum of *Passiflora incarnata* Extract

FT-IR Spectra of *Passiflora incarnata* Extract and F8 formulation were recorded. All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between drug and polymer. It also confirmed that the stability of drug during microencapsulation process.

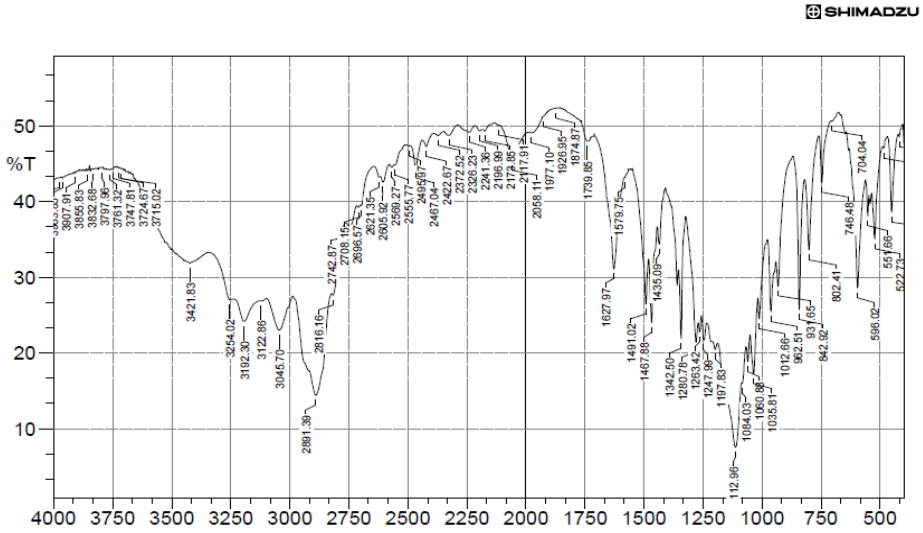

Fig-1: FT-IR Sample for*Passiflora incarnata* Extract

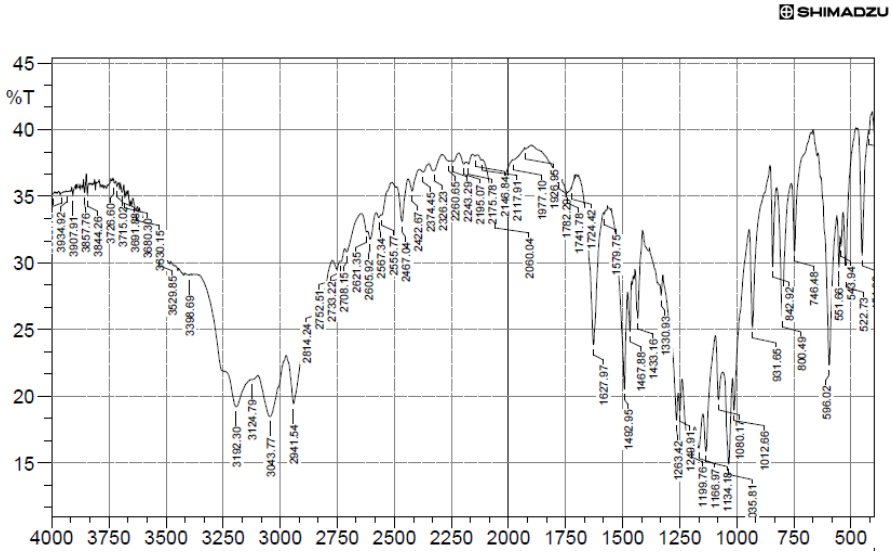

Fig-2: FT-IR Sample forOptimized formulation

Evaluation of Buccal formulation

Physical appearance:

The prepared buccal films were found to be uniform, smooth, flexible and homogenous.

Folding endurance:

The folding endurance numbers of all the *Passiflora incarnata* Extract buccal films are 170 – 188. The folding endurance number gives the mechanical property of the buccal films, high folding endurance number indicate that has high mechanical property. The folding endurance number was increased with increasing the polymer content. These results indicated that the buccal films would not break and maintain their integrity with general skin folding when applied.

Thickness of the films

Thickness was changed from batch to batch in individual strips of medicated films carry uniform thickness, which indicates that total medicated films carries uniform thickness.

Weight uniformity:

The weights are in the range of 156-163. The F6 formulation buccal films showed maximum weight.

Drug content:

The drug content analysis of the prepared formulations has shown that the process employed to prepare the buccal films was capable of giving uniform drug content with minimum batch variability.

Swelling index:

The swelling and hydration studies showed that the percent hydration varied from 45 to 64.

Table-2: Physicochemical evaluation of *Passiflora incarnata* Extract buccal films

F. code	Weight (mg)	Thickness (mm)	Folding endurance	Drug content (%)	% Moisture loss	% Moisture absorption	% Swelling index
F1	156	0.76	185	75.96	7.5	8.3	48
F2	160	0.81	178	74.82	7.9	8.1	51
F3	158	0.79	176	79.82	7.6	8.4	53
F4	159	0.83	181	80.13	7.7	8.7	49
F5	163	0.85	183	78.92	7.8	8.6	55
F6	160	0.87	179	82.36	7.1	8.9	47
F7	157	0.80	188.	76.38	7.4	9.1	52
F8	165	0.78	170	81.35	7.8	8.2	50

***In vitro* release study:**

Phosphate buffer pH 6.8 was used as medium for the release studies and good linearity was observed in the plotted standard graph with a correlation coefficient of 0.999. The drug release profiles of *Passiflora incarnata* Extract buccal films containing different ratios of synthetic polymer. It was cleared from the release profiles of formulations, that the drug release was governed by polymer nature and content.

In-vitro Dissolution Study

Table-3: *In vitro* drug release profiles of *Passiflora incarnata* Extract buccal films (F1-F8)

Time (min)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
0	0	0	0	0	0	0	0	0
15	16.89	17.10	18.12	17.40	18.10	19.64	18.49	17.25
30	27.53	28.10	27.82	29.52	30.13	32.16	30.15	29.84
45	37.13	38.16	39.68	34.13	41.26	46.35	45.13	43.12
60	46.89	48.13	49.60	46.82	50.18	53.48	50.38	52.14
120	55.67	56.98	57.14	59.17	63.54	67.84	65.12	61.57
180	75.60	76.35	77.60	75.86	79.85	76.82	77.25	75.48
240	83.65	85.16	83.64	82.19	83.15	85.46	83.10	84.52

300	92.34	93.30	94.75	95.36	96.89	98.10	97.46	95.36

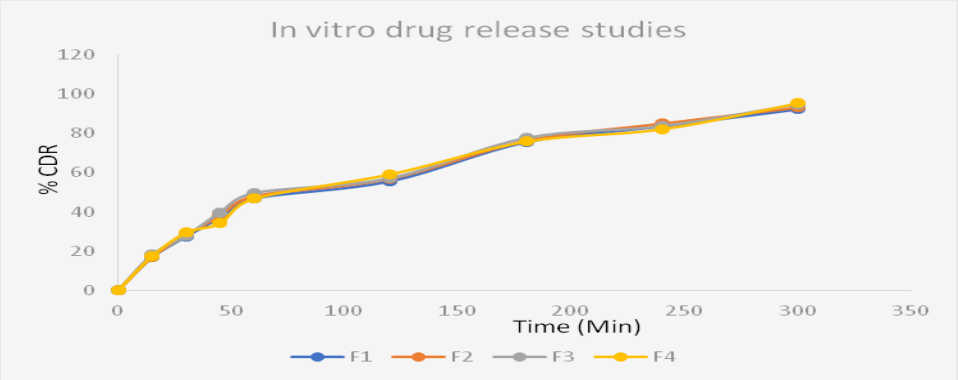

Fig-3: In vitro drug release studies of F1-F4 formulations

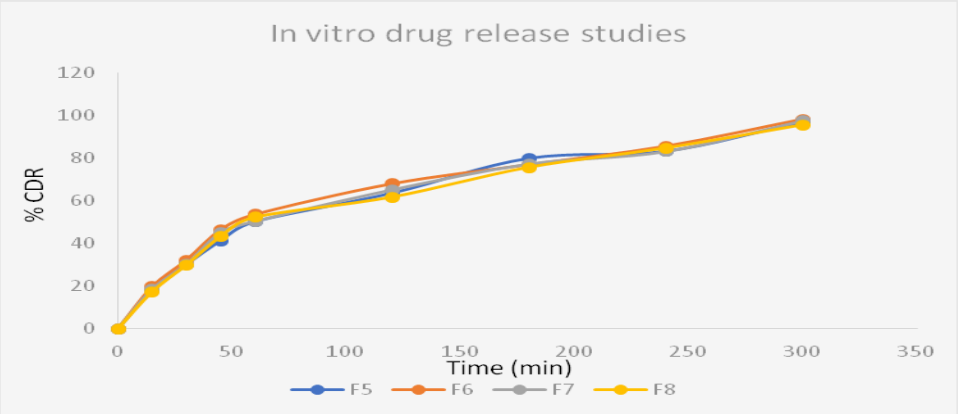

Fig-4: In vitro drug release studies of F5-F8 formulations

Kinetic modelling of drug release

All the 8 formulation of prepared buccal films of *Passiflora incarnata* Extract were subjected to in vitro release studies these studies were carried out using diffusion apparatus.

Zero order kinetics

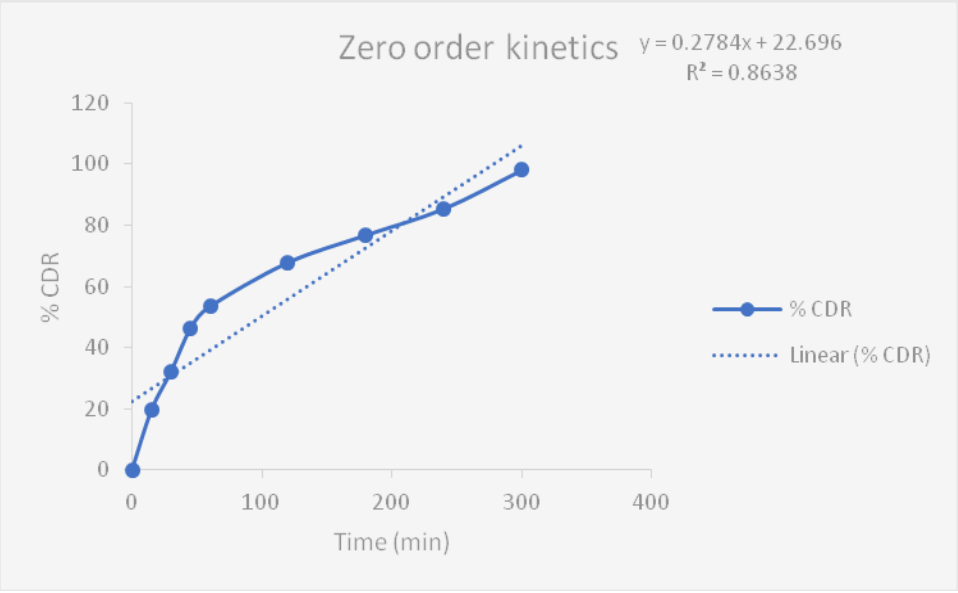

Fig-5: Zero order kinetics of optimized formulation

First order kinetics

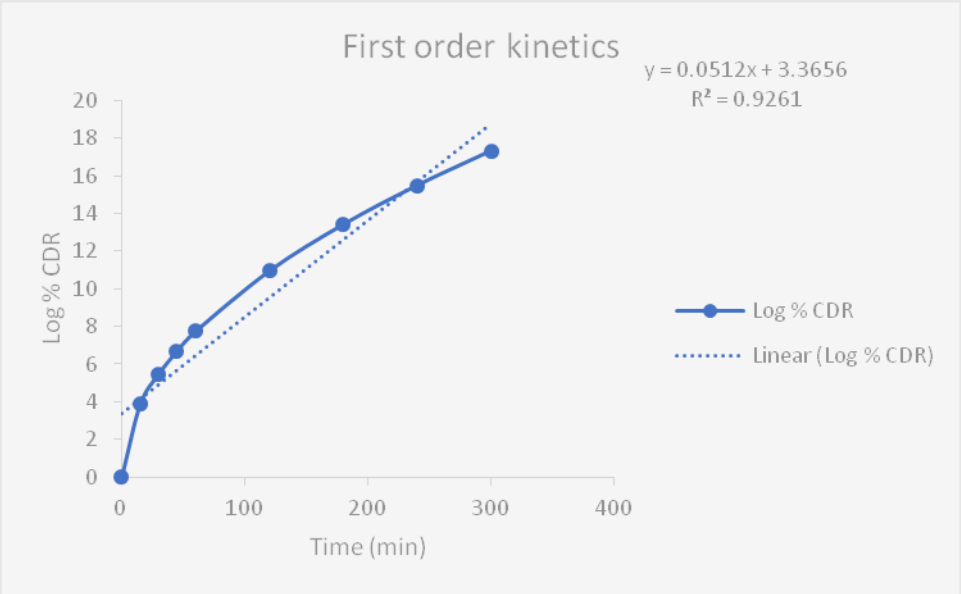

Fig-6: First order kinetics of optimized formulation

Higuchi model

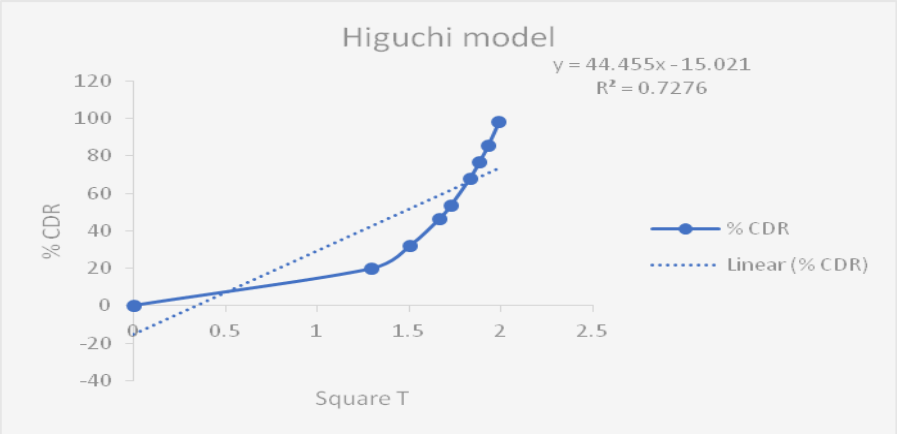

Fig-7: Higuchi model of optimized formulation

Korsmeyer peppas

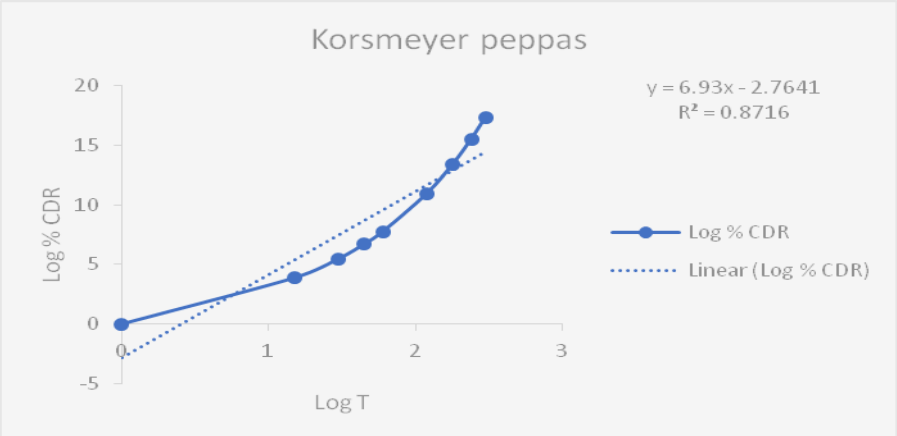

Fig-8: Korsmeyer peppas of optimized formulation

The kinetic values obtained for formulation F6 were shown. The values of in vitro release were attempted to fit into various mathematical models.

Regression values are higher with First order release kinetics. Therefore, all the *Passiflora incarnata* Extract buccal films

follows Korsmeyer peppas release mechanism.

Stability Studies

Table-4: Stability studies of optimized formulations at 40 ± 2 ^{0}C and 75 ± 5% RH for 3 months

Time in days	Drug content (%)	Folding endurance	Physical appearance	% Cumulative drug release
0	82.36	179	No change in color	98.10
90	81.58	178	Slight yellowish color	97.86

Phosphate buffer pH 6.8 was used as medium for the release studies and good linearity was observed in the plotted standard graph with a correlation coefficient of 0.997. The drug release profiles of *Passiflora incarnata* Extract buccal films containing polymer Ethyl cellulose. It was cleared from the release profiles of formulations, that the drug release was governed by polymer nature and content.

CONCLUSION

From this study it was concluded that the buccal Films containing *Passiflora incarnata* Extract can be successfully prepared by using release rate controlling polymers. Hence these formulations of *Passiflora incarnata* Extract buccal Films with having good permeability. Oral Mucoadhesive films of *Passiflora incarnata* Extract prepared using ethyl cellulose and HPMC polymers were found to be nonirritant with good mucoadhesion. These films could be effectively used to provide faster onset of action, increased bioavailability, and a prolonged drug release for *Passiflora incarnata* Extract. The sustained release that films provide can provide support for delayed emesis. Further, drug release rate from the films can be regulated by increasing either the content of hydrophilic or hydrophobic polymer within the film matrix.

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